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Urea transport through supported liquid membranes using synthetic carriers

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Abstract

Urea can be transported through a supported liquid membrane (Accurel/NPOE) by carriers such as metallomacrocycles and polyaza (cleft-type) receptors. The urea flux is increased by a factor 4–8 using polyaza receptors and by a factor 10–15 using metallomacrocycles containing a salophene unit in which a uranyl cation is incorporated. These carriers have a high hydrophobicity and do not significantly leak from the membrane phase into the aqueous phases. The structure of the receptors and the type and number of binding sites have a pronounced influence on the transport rate. The lower urea fluxes found for the polyaza (cleft-type) carriers are most likely caused by a weaker complexation (only H-bond interactions). No transport is observed for carriers which form *intra*molecular H-bonds. Although lower fluxes are obtained than with a commercial haemodialysis membrane (Cuprophan), the selectivity of transport may be much higher using carrier-mediated transport.

Key words: supported liquid membranes; carrier-mediated transport; urea transport; polyaza carriers; macrocycles

Introduction

Liquid membranes, especially supported liquid membranes consisting of an organic carrier solution immobilized in the pores of a porous polymeric support material, have been intensively used during the past decades for the selective transport of salts. Many types of macrocyclic receptors, e.g. crown ethers and calixarenes, can be used as selective carriers for the transport of cations through liquid membranes [1–5]. During the past decade there has been an increasing interest in the selective binding of neutral compounds. Complexes between neutral hosts and neutral guests are generally much weaker than complexes of neutral hosts with cations because the binding interactions (H-bonds, π–π stacking, and dipole–dipole interactions) are usually much weaker than the strong ion–dipole interactions in salt complexes. In addition the symmetry of neutral compounds is lower than that of spherical cations. This lower symmetry means that in complexes of neutral hosts and neutral guests shape complementarity is of great importance.

So far only a few examples have been re-

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ported of the transport of neutral compounds through organic bulk liquid membranes assisted by macrocyclic carriers like metalloporphyrins [6] (for amino acids) or macrobicyclic host molecules [7] (for nucleobases). More often, neutral compounds like small aromatic guest molecules are transported through an aqueous bulk liquid membrane using cyclophane-type carriers [8–10] or other macrocyclic receptors [11–14]. However, bulk liquid membranes require large quantities of solvent and carrier and are not suitable for technological applications. These disadvantages can be overcome by using supported liquid membranes.

Selective transport of neutral molecules is of importance in technological applications and the selective removal of urea from blood is an important issue in medicine. Haemodialysis membranes are used for this purpose but the selectivity of these membranes is mainly determined by the molecular weight of the transported species and not by specific interactions. Selective receptor molecules for urea that can be applied in membranes were until recently not available because most receptor–urea complexes are too weak, but recently strong and selective urea binders have been developed by Bell and Liu [15], Adrian and Wilcox [16], Hedge et al. [17], Hamilton [18], and Crego et al. [19]. In all these examples the receptor molecules are clefts having functional groups which form H-bonds with the urea or urea derivatives. Van Staveren et al. [20,21] found that incorporation of an electrophilic uranyl cation as a Lewis acid binding site in a macrocyclic receptor can result in a very strong interaction with polar neutral compounds. These metallomacrocycles containing a salophene moiety complex urea by coordination of the urea carbonyl oxygen atom to the uranyl cation, which is bound to the salophene moiety, and by hydrogen bonding between the NH_2 functions of urea and the oxygen atoms of the ethylene glycol bridge of the host [22] (see Fig. 1). The solubility as well as the hydrophobicity of these carriers were improved by incorporating binaphthyl or calix[4]arene groups in these metallomacrocycles [23].

It was found that several of these metallomacrocyclic receptors transport urea through supported liquid membranes and this represents the first example of transport of neutral compounds through supported liquid membranes assisted by macrocyclic carriers [24]. In this paper we describe the results of the transport of urea through supported liquid mem-

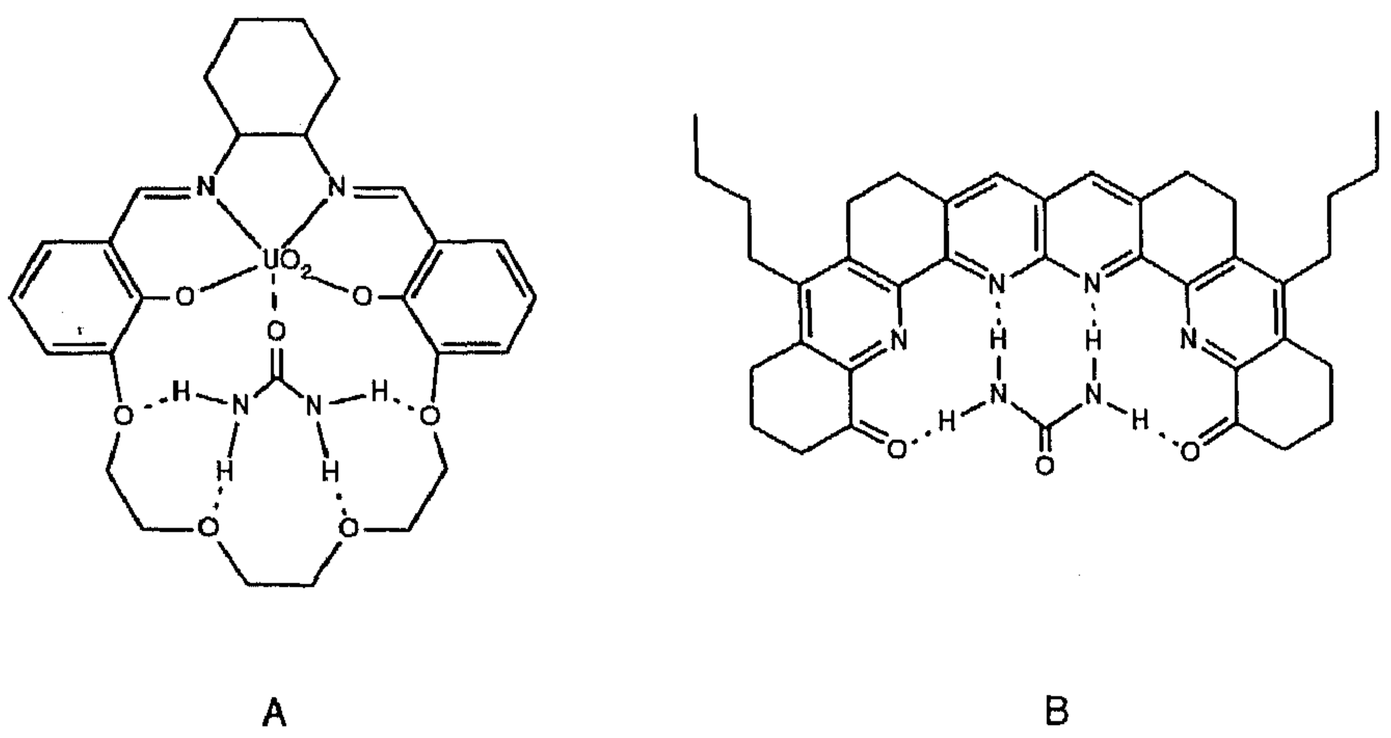


Fig. 1. Urea complexes of a metallomacrocyclic receptor (A) and a polyaza receptor (B) [15].

branes assisted by different types of urea receptors as carriers and in particular the relation between the carrier structure and the transport rate. Different types of polyaza and, in most cases, cleft-type receptors were incorporated and the results were compared with transport assisted by metallomacrocyclic carriers and using a commercial haemodialysis membrane (Cuprophan). In these polyaza receptors, the urea molecule is complexed by H-bonds with the receptor (see Fig. 1).

Experimental

The synthesis of the compounds **1–10** has been described elsewhere or will be published in the near future [15,17,23,25,26]. Urea and *p*-(N,N-dimethylamino)benzaldehyde were obtained from Janssen Chimica and were used as received. The polymeric film Accurel® was obtained from Enka Membrana. *o*-Nitrophenyl n-octyl ether was obtained from Fluka and was used without further purification.

The transport experiments were carried out in a permeation cell consisting of two identical cylindrical compartments (half-cell volume: 50 mL; effective membrane area: 12.4 cm^2). Details of this cell have been described elsewhere [27] (see Fig. 2). The supported liquid membrane consisted of a thin microporous polypropylene film (Accurel®; thickness $d=100$ μm, porosity 64%) immobilizing the solution of carrier in *o*-nitrophenyl n-octyl ether (NPOE). Aqueous urea solutions were used as the source phase. Doubly distilled and deionized water was used as the receiving phase. The measurements were performed at 25°C and at least in duplicate. Samples of the receiving phase were taken after 24 hr (unless stated otherwise) and the concentration of urea was determined by UV/Vis spectroscopy. The standard deviation in urea concentration during the transport experiments is about 15%.

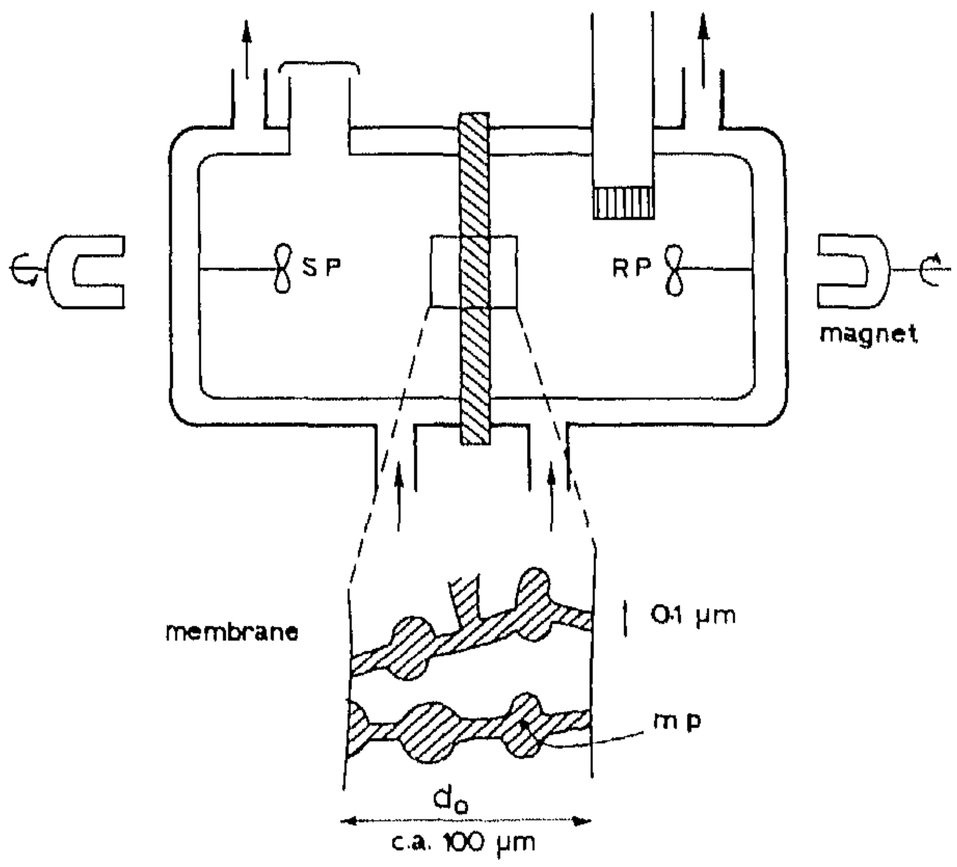


Fig. 2. Schematic representation of the supported liquid membrane measurement set-up.

The urea concentration in the receiving phase was determined by UV/Vis spectroscopy [28–30]. A stock solution of *p*-(N,N-dimethylamino)benzaldehyde was prepared by dissolving 8 grams in 400 mL of ethanol (99.5%) and 40 mL of concentrated HCl. Small amounts of aqueous urea solutions of known concentration were added to 10 mL of this stock solution and the solution was diluted with bidistilled and deionized water until the total volume was 25 mL. The UV/Vis absorption was measured at 435 nm using a Uvikon 930 spectrophotometer and a blank solution of 10 mL of stock solution diluted to 25 mL with doubly distilled deionized water. In this way a calibration curve was obtained for urea concentrations from 0.1 m*M* to 2 m*M*. After 24 hr of transport (unless stated otherwise) 15 mL of the receiving phase was added to 10 mL of the stock solution and the concentration was determined by measuring the absorption at 435 nm and using the calibration curve.

Results and discussion

Previously [24] we have described a model

for the diffusion-limited, carrier-mediated transport of neutral molecules through a supported liquid membrane. The flux (J_{ass}) caused by the carrier-assisted transport (when no leaking of the carrier from the membrane phase is observed) is expressed as:

$$J_{ass} = \frac{D_m K_{ex} [U]_w^0 [CA]_m^0}{d(1 + K_{ex}[U]_w^0)} \quad (1)$$

which shows that the urea flux depends on the diffusion coefficient of the complex (D_m), the membrane thickness (d), the extraction constant (K_{ex}), the initial urea concentration in the source phase $[U]_w^0$, and the initial carrier concentration in the membrane phase $[CA]_m^0$.

Polyaza receptors **1–8** were used to transport urea through a supported liquid membrane (Fig. 3).

These carriers were used in a supported liquid membrane composed of a carrier solution in *o*-nitrophenyl n-octyl ether (NPOE) immobilized in a porous polymeric support (Accurel® to investigate the relation between the structure of the carrier and the rate of urea transport. The transport rates were compared with those obtained using metallomacrocycles **9,10** (Fig. 4). The membrane separates the aqueous urea containing source phase (s.p.) from the aqueous receiving phase (r.p.) which initially contains no urea. The urea transport was monitored after 24 hr (unless stated otherwise) by UV/Vis analysis at 435 nm of the complex formed between urea and *p*-(N,N-dimethylamino)benzaldehyde (added to a sample of the receiving phase), following literature procedures [28–30]. A 1 *M* urea solution was used as the source phase and a 6.0 m*M* carrier solution in NPOE.

The results of the transport measurements are listed in Table 1. In absence of carrier the urea flux (blank flux) is low. Carriers **1** and **2** show no significant transport, the urea flux measured is comparable to the blank flux. In these receptors the binding of urea in the cleft is hindered by intramolecular H-bonding of the carrier [25]. This is not the case for compounds **3**, **4**, and **5** which form four hydrogen bonds with urea and which show a good and quite stable urea transport. The central pyridine nitrogen of **3** results in a lower extraction constant because of electrostatic repulsion with the carbonyl oxygen of urea [25] and therefore

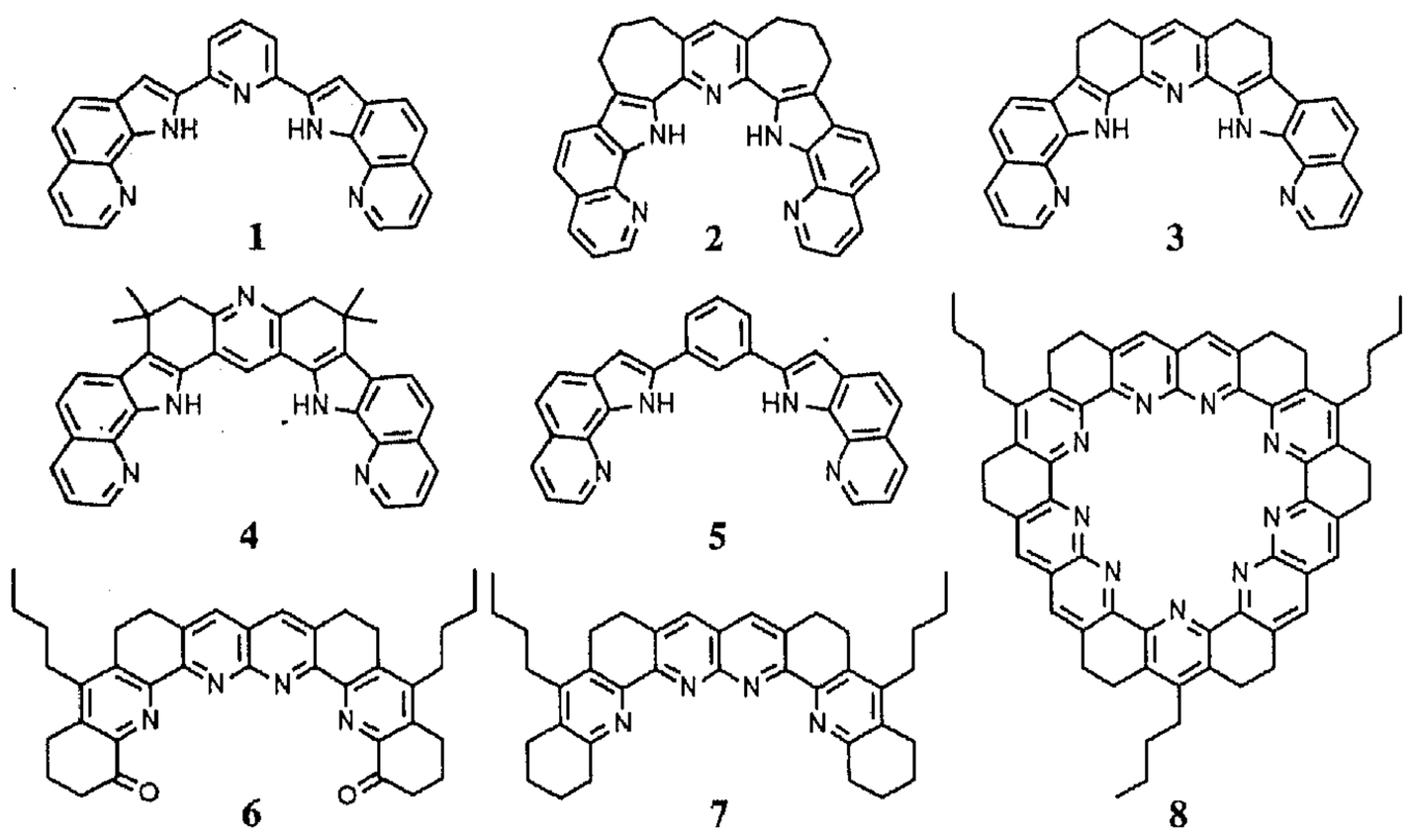
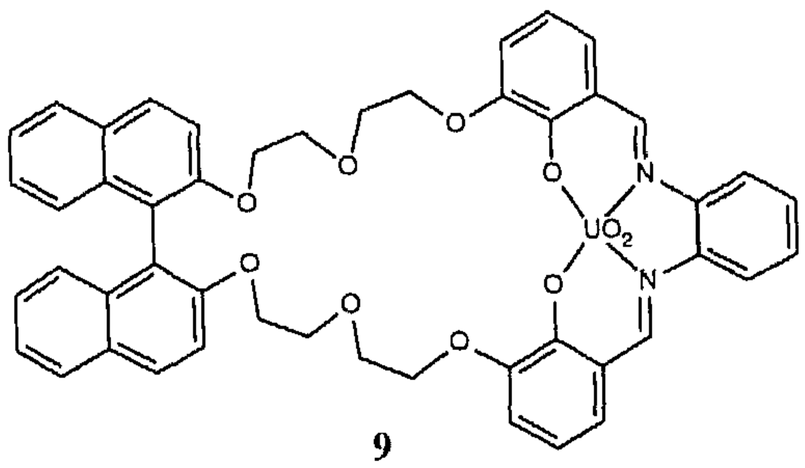


Fig. 3. Polyaza (cleft-type) receptors used as urea carriers in a supported liquid membrane.



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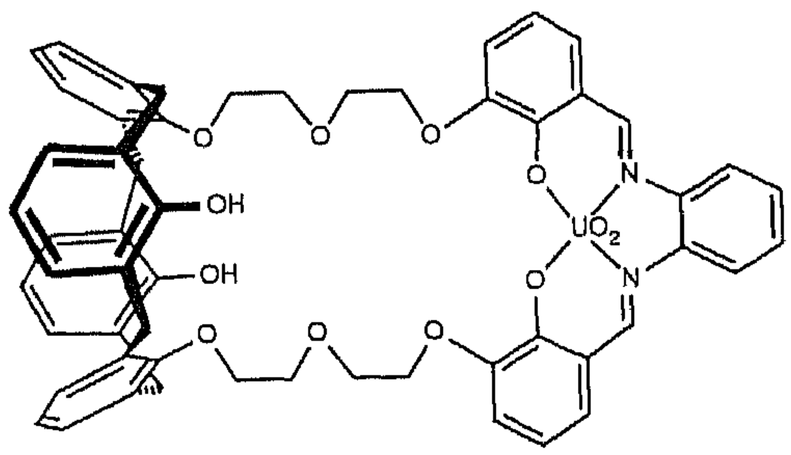

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Fig. 4. Metallomacrocycles used as urea carriers in a supported liquid membrane.

TABLE 1

Total urea fluxes[a] through a supported liquid membrane measured for different types of urea carriers

Carrier	Carrier conc. (m*M*)	Flux (10^{-8} mol-m^{-2}-sec^{-1}) no. of replacements[b]		
		0	1	2
–	–	4.4	–	–
1	6.0	5.0	6.9	–
2	6.0	5.8	5.6	–
3	6.0	21	17	–
4	6.0	25	23	24
5	6.0	36	36	36
6	6.0	16	14	14
7	6.0	5.8	–	–
8	6.0	6.4	–	–
9	6.0	61	64	64
10	5.9	50	50	50

[a] $[\text{urea}]_w^0 = 1\ M$.

[b] Replacements of the receiving phase after 24 hr.

in a somewhat lower flux (see eqn. 1). The most flexible carrier **5** shows the highest transport rate. In this case the urea transport is more than 8 times higher than the blank flux, but is somewhat lower than the urea fluxes measured for the metallomacrocyclic carriers **9** and **10**.

In compound **6** the urea forms H-bonds with the carbonyl groups of the receptor [15] (in addition to the H-bonds formed between the NH_2 functions of urea and the pyridine nitrogens) and a small urea flux was measured. This is not the case for carriers **7** and **8** for which no significant urea transport was observed. In all these receptors **1–8** the interactions with urea are based on H-bonds. In all cases the fluxes obtained were lower than the ones for metallomacrocyclic carriers. This is in agreement with complexation data (assuming that the diffusion coefficients are of the same order of magnitude as for the metallomacrocycles, see eqn. 1) which show that in $CDCl_3$ the urea complexes of metallomacrocycles containing a uranyl cation are $\geqslant 5000$ times more stable than the **6**$\cdot$–urea complex [22]. This clearly shows that the strong uranyl–urea carbonyl coordination contributes to the strong binding of urea to the metallomacrocyclic carriers and therefore to the high urea fluxes obtained. These results also show that the urea flux is the greatest when there is maximum complementarity between the binding sites of host and guest (compare compound **6** to compounds **7** and **8**).

Table 1 also shows that upon replacing the receiving aqueous phase one and two times respectively, hardly any significant decrease in flux is obtained for all the carriers used. This implies that all the carriers used are hydrophobic enough for the system used to remain in the membrane phase and result in a stable membrane (for more than 2 weeks).

The performance of the supported liquid membranes was compared to the urea transport through a commercially available dialysis membrane (Cuprophan, $d = 10\ \mu$m). In this case

a urea flux of 9×10^{-5} mol-cm^{-2}-hr^{-1} was observed (using a 50 m*M* solution of urea in water as the source phase) compared to a total flux of 13×10^{-8}-cm^{-2}-hr^{-1} using a 6.0 m*M* solution of binaphthyl carrier **9** in NPOE/Accurel. However, the transport through a dialysis membrane is much less selective since separation is mainly based on molecular weight instead of specific interactions as in carrier-mediated transport. The membrane thickness of the dialysis membrane is also smaller (10 μm) than for Accurel (100 μm). The carrier-assisted transport might be improved by using thinner support materials and higher carrier concentrations in the membrane phase (see eqn. 1).

Conclusions

Neutral compounds like urea can be transported by different types of macrocyclic or cleft-type carriers through supported liquid membranes. High carrier loading can be obtained using hydrophobic metallomacrocyclic carriers (which have a strong interaction with urea via H-bonds as well as coordination of the urea carbonyl to the uranyl cation). Polyaza, cleft-type receptors in which the interaction with urea is based on H-bonds only and which do not possess a uranyl cation also transport urea, although the observed flux is lower than for the metallomacrocyclic carriers. In this case the urea flux decreases with decreasing complementarity between the binding sites of host and guest.

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